CLAIMS

What is claimed is:

1. A process for producing a target delivery molecule, which comprises:

(a) synthesizing a target molecule complex comprising (a') a bridging agent selected from the group consisting of a transition element, an inner transition element, a neighbor element of said transition element and a mixture of any of the foregoing elements; and (b') a complexing agent; provided that when said transition element is chromium a chromium target molecule complex is synthesized; and

(b) combining said target molecule into a liposomal matrix to form the target delivery molecule.

2. The process as defined in claim 1 wherein steps (a) and (b) are simultaneously carried out in situ.

3. The process of claim 1, wherein said liposomal matrix comprises a charged liposomal structure.

4. The process of claim 1, wherein said chromium target molecule complex is prepared by a method comprising

(a) combining an aqueous solution of N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid having an pH between 3.2 and 3.3 with an aqueous solution of a chromium compound having a pH between 4.0 and 4.4 to form a reaction solution;

(b) maintaining the reaction solution at a pH between 3.2 and 3.3 to form a complex solution; and

(c) incubating said complex solution to form said chromium complex.

5. A target delivery molecule produced by the process of claim 1.

6. The process of claim 1 which further comprises the step of combining a pharmacological agent with the target delivery molecule to form a pharmacological delivery system.

7. A target delivery molecule produced by the process of claim 6.

8. The target delivery molecule of claim 7, wherein said pharmacological agent is encompassed by the liposomal matrix or entrapped in the liposomal core volume.

9. The target delivery molecules of claim 7, wherein said pharmacological agent comprises insulin or a derivative thereof.

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10. The target delivery molecule of claim 7 wherein said agent comprises seratonin.

11. The target delivery molecule of claim 7, wherein said liposomal matrix comprises distearoyl lecithin, cholesterol and dicetyl phosphate.

12. The target delivery molecules of claim 11, wherein said pharmacological agent is selected from insulin, a derivative of insulin, and seratonin.

~~13.~~ An hepatocyte targeting molecule, comprising

(a) a liposomal membrane; and

(b) a target complex comprising (a') a bridging element or a dissociated moiety of thereof or a polynuclear complex or a mixture of the foregoing, where said dissociated moiety exists with or without metal in the liposomal membrane; and (b') a complexing agent; provided that when said bridging element is chromium a chromium target molecule complex as shown in Figure 2 is present in the hepatocyte targeting molecule.

14. The hepatocyte targeting molecule of claim 13 wherein said complexing agent comprises N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid.

15. The hepatocyte targeting molecule of claim 13 wherein said liposomal membrane comprises a lipid selected from distearoyl lecithin, cholesterol, dicetyl phosphate and a mixture of the foregoing lipids.

16. The hepatocyte targeting molecule of claim 15 wherein said liposomal membrane comprises a mixture of distearoyl lecithin, cholesterol and dicetyl phosphate.

17. The hepatocyte targeting molecule of claim 16 wherein said distearoyl lecithin is present in an amount of about 25.5 micro moles/ml, said cholesterol is present in an amount of about 6.85 micro moles/ml and said dicetyl phosphate is present in an amount of about 9.4 micro moles/ml with 0.465 micro moles/ml of chromium complex.

~~18.~~ An article of manufacture for delivering an agent in liposomal form to the hepatocytes in the liver containing first member comprising a chromium target molecule complex or a dissociated moiety thereof, said first member being soluble in a second member comprising a liposome which is capable of carrying the agent, wherein said first member is specific for cellular hepatocytes, exhibits a maximum visible absorption spectrum at 5250 Å, is soluble in organic solvents and has a first

structural component which is chromium and a second and a third structural component comprising at least one complexing agent or a mixture of complexing agents.

19. The article of manufacture of claim 18 wherein said complexing agent comprises N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid.

20. The article of manufacture of claim 18 wherein the agent comprises a therapeutic agent.

21. The article of manufacture of claim 18 wherein the agent comprises a diagnostic agent.

22. A liposomal delivery system directed to hepatocytes of a warm-blooded host comprising a liposome, at least one bridging agent complex which is insoluble in water and soluble in said liposome and an active agent destined to be delivered to the hepatocytes which is carried by said liposome.

23. The system of claim 22 wherein said active agent is a therapeutic agent.

24. The system of claim 22 wherein said active agent is a diagnostic agent.

25. The system of claim 22 wherein said bridging agent complex comprises a chromium target molecule complex or a dissociated form thereof.

26. The system of claim 25 wherein said chromium. target molecule complex is complexed with N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid.

27. The system of claim 22 wherein said active agent is insulin or a derivative thereof.

28. The system of claim 22, wherein said active agent comprises an insulin derivative, said derivative being composed of a single or several combinations of monomeric insulin subunits ranging in composition from one monomeric subunit to nine associated monomeric subunits or a combination thereof, wherein at least one of said derivatives preferentially loads into the core or into the membrane or onto the surface of said liposome for delivery to the hepatocytes in the liver of a warm-blooded host.

29. A process for producing a hepatocyte directed vesicle comprising the steps of:

(a) reacting chromium with N-(2,6-diisoproplyphenylcarbamoylmethyl) iminodiacetic acid to form a chromium target molecule complex; and

(b) adding the chromium target molecule complex to a liposome to form the hepatocyte directed vesicle.

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30. The hepatocyte directed vesicle produced by the process of claim 29.

~~31.~~ A process for producing a hepatocyte directed vesicle comprising the steps of:

(a) reacting a suitable metal selected from a transition metal other than chromium, an inner transition metal, a neighbor metal of said transition metal and a mixture of any of the foregoing metals with a suitable complexing agent to form a target molecule complex; and

(b) adding said complex to a liposome to form a hepatocyte directed vesicle.

~~32.~~ A composition for delivering an active agent to a target site in a mammal which comprises, a transport agent comprising a liposome having associated therewith a bridging agent selected from a metal complex, a dissociated form thereof or a polynuclear complex or a mixture of any of the foregoing; where said dissociated form exists with or without metal present in said liposome; provided that when compound chromium is used, it is present as a chromium target molecule complex or a dissociated form thereof.

33. The composition as defined in claim 32 wherein said liposome comprises a lipid selected from distearoyl lecithin, cholesterol, dicetylphosphate and a mixture of any of the foregoing lipids.

34. The composition as defined in claim 33 wherein said liposome comprises a mixture of distearoyl lecithin, cholesterol, and dicetyl phosphate.

35. The composition as defined in claim 32 which further comprises an active agent associated with said liposome.

36. The composition as defined in claim 35 wherein said active agent is selected from insulin, a derivative thereof, or seratonin.

~~37.~~ A chromium complex which is prepared by a method comprising

(a) combining an aqueous solution of N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid having an pH between 3.2 and 3.3 with an aqueous solution of a chromium compound having a pH between 4.0 and 4.4 to form a reaction solution;

(b) maintaining the reaction solution at a pH between 3.2 and 3.3 to form a complex solution; and

(c) incubating said complex solution to form the chromium complex.

38. The complex of claim 37, wherein said chromium compound is chromium (III) chloride hexahydrate.

39. A water-insoluble hepatocyte targeting complex comprising chromium (bis)[N-2,6-diisopropylphenylcarbomoylmethyl)iminodiacetic acid].

40. An organic soluble chromium target molecule complex formed by combining N-(2,6-diisopropylphenylcarbamoylmethyl)iminodiacetic acid and chromium (III) chloride which demonstrates targeting ability for the hepatocytes of the liver in a warm-blooded host.

41. The complex of claim 40 wherein an atom of chromium is bound to two molecules of said iminodiacetic acid and is insoluble in aqueous media.